PATENT SPECIFICATION

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COMPLETE SPECIFICATION

Improvements in or relating to Preparation of 3-Keto Steroids having Cis Junction of Rings A and B

We, THE GLIDDEN COMPANY, a corporation organised under the laws of the State of Ohio, United States of America, of 1396, Union Commerce Building, Cleveland, Ohio, United States of America, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention relates to a process for preparing 3-keto steroids having a cis junction of rings A and B. More particularly, this invention relates to a process for reducing 3-keto-Δ^4-steroids (excluding steroids containing an 11-keto group) in the presence of a palladium catalyst and in the presence of an inorganic base and in an anhydrous medium.

The recent discovery of the beneficial effects of cortisone, 4-pregnene-17α,21-diol-3,11,20-trione, and related hormones of the adrenal cortex in the treatment of rheumatoid arthritis and other diseases has intensified efforts designed to improve the partial syntheses of these hormones from readily available steroidal raw materials. Currently, cortisone is synthesized from desoxycholic acid which is obtainable largely from ox bile. However, the supply of ox bile is limited and attention now is being directed to the utilization of more plentiful steroidal materials. Most promising among such other raw materials are stigmasterol, which is obtainable from soya sterols, and diosgenin, which is a saponin obtainable from Mexican root sources. Desoxycholic acid differs essentially from the above-mentioned more readily available sterols in the presence of a 12-hydroxyl group and in the absence of a double bond at positions 5, 6. Further, rings A and B of the bile acids are cis locked (i.e., the hydrogen at the 5-position is cis with respect to the methyl group C_{19}), whereas the reduction by known means of the 5, 6 double bond of stigmasterol, diosgenin or degradation products thereof lead to A/B trans or allo junctions, or at best difficultly separable mixtures of the two geometric isomers.

Palladium catalysts have been used in neutral media to reduce 3-keto-Δ^1-steroids for the purpose of obtaining 3-keto-A/B-cis compounds. For Example, Grasshof, Z. physik. chemie, *223*, 251 (1934), has described the catalytic reduction of cholestenone in ether in the presence of palladium black. This reduction resulted in a mixture from which the coprostanone was separated from the allo by-products by means of digitonin and careful fractional crystallization. Progesterone, when reduced in a neutral methanol medium in the presence of palladium catalyst, results in approximately equal amounts of allopregnan-3,20-dione and pregnan-3,20-dione. It was thus surprising that in the presence of an inorganic base and in an anhydrous medium, the stero-chemical course of this reduction could be altered to the extent that a practically complete conversion to the 3-keto-A/B-cis derivative occurs and substantially none of the allo compound is obtained.

Accordingly, it is an object of this invention to devise a means for preparing steroids having a cis junction at rings A and B.

A further object is to provide a process for the catalytic reduction of 3-keto-Δ^4-steroids in the presence of a palladium catalyst and in the presence of an inorganic base to reduce the 4-5 double bond. One such steroid according to the invention comprises a 3-keto-10,13-dimethyl-Δ^4-steroid.

A more specific object of this invention is to prepare a product comprising 7-pregnen-3,20-dione from 4,7-pregnadien-3,20-dione, and also to prepare the product comprising 3-keto-bisnor-7-cholenic acid and 3-keto-bisnor-cholanic acid and esters thereof.

It is also an object of this invention to use starting steroids which are pregnenes, stenones (the keto analogues of unsaturated sterols e.g. cholestenone, stigmastenone etc.), steroids of the C_{17} series, of the C_{28} series, steroids containing a double bond in the 7-8 position, steroids in which the 3-keto group is the sole

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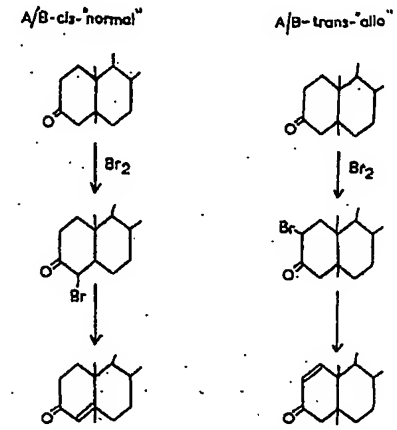
keto group attached to the polyhydrocyclopentanophenanthrene nucleus of the steroid, or $\Delta^{4,7}$-pregadiene-dione-3,20 and the 20-cyclic ketal derivatives derived from alkylene glycols.

These objects are attained by the catalytic reduction of 3-keto-Δ^4-steroids (excluding steroids containing an 11-keto group) in the presence of a palladium catalyst and in the presence of an inorganic base and in an anhydrous medium. We have found that under such conditions, a practically complete stereo specific conversion to the isomer in which rings A and B are cis locked is obtained, i.e. a 3-keto-A/B-cis-steroid substantially free of the allo isomer. This surprising result has been obtained even in those instances where the compound being reduced contains additional keto groups or non-conjugated double bonds elsewhere in the nucleus. For example, 7-dehydroprogesterone, on being reduced by our novel process, is converted practically completely to 7-pregnen-3,20-dione. Isoergosterone gives coproergost-22(23)-en-3-one, methyl 3-keto-$\Delta^{4,7}$-bisnorcholadienate is reduced to methyl 3-keto-Δ^7-bisnorcholenate, and $\Delta^{4,7,9(11)}$-pregnatriene-3,20-dione yields $\Delta^{7,9(11)}$-pregnadien-3,20-dione.

As indicated by the reduction of isoergosterone, which is obtained from ergosterone by treatment with dry hydrogen chloride, Barton, Cox and Holness, J.C.S., 1773 (1949), a nuclear double bond conjugated with the 3-keto-Δ^4 system is reduced in accordance with our invention. Whereas non-conjugated double bonds, whether present in Ring B or elsewhere in the sterol molecule, are not affected, the nuclear conjugated bonds are reduced completely, resulting in 3-keto-A/B-cis derivatives.

3-Keto-A/B-cis steroids are useful intermediates in newly devised syntheses of many therapeutically valuable steroid products from vegetal sterols. For example, 11-keto steroids, and from these cortisone, can be synthesized from stigmasterol by a series of reactions involving the novel stereospecific reduction of our invention, i.e. the reduction of methyl 3-keto-$\Delta^{4,7,9(11)}$-cholatrienate to the corresponding $\Delta^{7,9(11)}$-diene. It is desirable to effect this reduction step prior to the introduction of the 11-keto group inasmuch as this latter step involves the use of reagents which can react also with the 3-keto-Δ^4-conjugated system. In fact, the 3-keto-Δ^4-system is more reactive in some instances than the $\Delta^{7,9(11)}$-system. Moreover, it has been found that the reduction of 3,11-diketo-Δ^4 steroids produces anomalous results, e.g., the stereochemical course of the reaction is altered, giving rise to allo derivatives in part. Thereafter, reintroduction of the Δ^4 double bond is effected more readily and in better yield with the A/B cis isomers than the A/B trans compounds, the latter on treatment with one mol of bromine leading to an appreciable amount of the 2-bromo derivative rather than the desired 4-bromo derivative, as indicated by the following formulae:



The following examples will illustrate the process of our invention:

EXAMPLE I

Production of Pregnan-3,20-Dione

A) Preparation of Catalyst:

To 32 cc. of a 1% aqueous solution of palladium chloride 0.38 grams of activated charcoal was added while swirling. The mixture was boiled gently under reflux for 10 minutes and then after being cooled, it was transferred to a hydrogenation apparatus and reduced therein with hydrogen. The mixture was filtered and the pyrophoric filter cake was washed with water and then with methanol.

B) Reduction of Progesterone:

The catalyst mixture prepared above was transferred to a hydrogenation apparatus and mixed therein with 1 g. of progesterone dissolved in 18 cc. of methanol. 0.2 g. of potassium hydroxide in 15 cc. of methanol was added and the mixture was reduced with hydrogen. After 45 minutes, slightly less than 1 mol equivalent of hydrogen had been absorbed and the hydrogenation was stopped.

The mass was filtered from the catalyst and water was added to the filtrate to precipitate the dissolved material. The resultant slurry was filtered and dried. m.p. of crude 108° to 114° C.

The crude product was dissolved in 2 cc. of benzene and the solution filtered. An equal volume of petroleum ether was added. No precipitate of "allo" isomer was obtained on cooling. The mixture was then concentrated to a syrup. 4 cc. of petroleum ether were added and the cloudy solution was cleared up with a minimum of benzene. On cooling, 0.73 g. of pregnan-3,20-dione crystallized. On mixmelting a portion of this material, m.p. 111° to 119° C., with an authentic sample of pregnan-3,20-dione, m.p. 118° C., no lowering of the melting point was observed.

EXAMPLE II

REDUCTION OF 7-DEHYDROPROGESTERONE

Catalyst prepared from 32 cc, of 1% aqueous palladium chloride and 0.38 g. of charcoal as described in Example 1-A. Thereafter 1 g. of 7-dehydroprogesterone, prepared as described in Journal of Organic Chemistry 16, 1456 (1951), in 15 cc. of methanol was added. The hydrogenation was permitted to proceed until slightly more than 1 mol equivalent of hydrogen was absorbed. The reaction mixture was filtered and the filtrate, after dilution, was extracted with ether. The ethereal extract was washed alkali-free and evaporated to dryness. The crude product comprising Δ^7-pregnene-dione-3,20 melted at 140° to 150° C. Its UV absorption spectra showed no peak characteristic of Δ^7-progesterone. A similar reduction carried out in a caustic soda alkaline medium resulted in a product which, on recrystallization from acetone, melted at 153° to 154° C.

The 20-cyclic ethylene ketal of 7-dehydroprogesterone was reduced in a caustic soda alkaline medium in a similar manner and gave a product melting at 165° to 166° C., from ether-petroleum ether. The product, comprising 20 cyclic ethylene ketal of Δ^7-pregnene-dione-3,20, on hydrolysis with sulfuric acid in methanolic solution, in the manner described in J.A.C.S. 72, 367 (1950), gave a product melting at 154° to 156° C., from ether-petroleum ether. On being mix-melted with 7-pregnen-3,20-dione, prepared above by reduction in an alkaline medium, no depression in the melting point was observed.

EXAMPLE III

REDUCTION OF ISOERGOSTERONE

1.0 g. of isoergosterone in 10 cc. of benzene was added, using 7 cc. of methanol as wash, to a catalyst mixture prepared as above from 3.2 cc. of 1% aqueous palladium chloride and 3.8 g. of charcoal and 0.25 g. KOH in 13 cc. of methanol. This mixture was reduced with hydrogen and after 90 minutes, just less than 2 mol equivalents of hydrogen were taken up.

The mixture was filtered and the catalyst was washed with benzene. The clarified filtrate was diluted with ether and this mixture was washed with water. After drying, the solution was evaporated to dryness. The residue was crystallized from a mixture of acetone and methanol. 0.84 g. of crude product melting at 106° to 110° C. was obtained, which, upon recrystallization, melted at 110.5° to 11.5° C. The product was thusly identified as coprogergost-22(23)-en-3-one, see Barton, Cox and Holness, J.C.S., 1771 (1949).

EXAMPLE IV

PREPARATION OF METHYL 3-KETO-BISNOR-7-CHOLENATE

A) Preparation of Methyl 3-Keto-bisnor-4,7-Choladienate:

5 g. of methyl 3β-hydroxybisnor-5,7-choladienate dissolved in 215 ml. of toluene and 45 ml. of cyclohexanone was distilled. After about 25 ml. of distillate was collected, 2.15 g. of aluminum isopropylate in 21.5 ml. of dry toluene was added dropwise in 3 minutes to the refluxing mass. After ½ hour, 0.65 ml. of glacial acetic acid in 6 ml. of toluene was added and the resultant mixture was distilled with steam. The distilland was cooled, diluted with water and extracted with two portions of 500 ml. each of ether. The ether extract was washed with succcessive portions of 10% HCl, water and 10% NaOH. The washed extract was concentrated and the residue dissolved in methanol. From the methanol solution 2.86 g. of green-yellow prisms melting at 143° to 145° C. were obtained.

B) Reduction of Methyl 3-Keto-bisnor-4-7-choladienate:

Catalysts prepared as described in Example I—A above from 16 ml. of 1% aqueous palladium chloride was transferred to a hydrogenation bottle using 25 ml. of methanol. 1 g. of potassium hydroxide dissolved in 50 ml. of methanol and 5 g. of the 3-keto ester prepared in Example IV—A dissolved in 20 ml. of methanol were added. The mixture was hydrogenated until just less than 1 mol equivalent of hydrogen was absorbed. Thereafter, the mixture was filtered and the clarified filtrate, after being concentrated to about ½ its volume, was diluted with water. The mixture was rendered acid with dilute hydrochloric acid and then extracted with two 100-ml. portions of ether. The extract was washed twice with aqueous sodium carbonate, five times with water and the washed extract was dried over sodium sulfate. The solution was concentrated to a syrup and the residue diluted with a small quantity of methanol. The red solution was clarified by warming, decolorizing charcoal added and after several minutes the mixture was filtered. The filtrate was evaporated to a volume of about 30 ml. and permitted to stand. 2.4 g. of yellow needles melting at 125° to 129° C. were obtained. The crude material was recrystallized from methanol and the resultant white prisms showed no absorption between 350 mμ and 250 mμ. Emax at 214 mμ = 2252. The product resulting from the reduction step comprised methyl 3-keto-bisnor-7-cholenate.

EXAMPLE V

PREPARATION OF METHYL-3-KETO-BISNOR-CHOLANATE

A) Preparation of Methyl 3-Keto-bisnor-4-Cholenate:

A mixture of 25 g. of methyl 3-hydroxybisnor-5-cholenate, 1075 ml. of toluene and 225 ml. of cyclohexanone was dried by distilling off about 50 ml. of toluene. The mass was refluxed as a solution of 6.75 g. aluminum

isopropylate in 107.5 ml. of toluene was added dropwise during about 5 minutes. The mixture was refluxed for ½ hour and then 3.25 ml. of acetic acid in 30 ml. of toluene were added.

The mixture was cooled, diluted with 5% aqueous hydrochloric acid and then extracted with ether. The ethereal solution was washed with successisve portions of 5% hydrochloric acid, water, 10% aqueous caustic soda and water until neutral. The extract was evaporated under vacuum to remove most of the solvent and the residue was distilled with steam until 5 l. of distillate were collected. The distilland was extracted with ether and the extract was washed with water. After being dried, the extract was concentrated until a saturated solution of the product was obtained. Thusly, 16.97 g. of material, m.p. 177° to 180° C., were separated by filtration of the resultant cooled solution. Emax at 242 mμ = 17,304.

B) Reduction of Methyl 3-Keto-bisnor-4-cholenate:

Catalyst obtained as described above in Example 1—A from 32 ml. of 1% palladium chloride was transferred to a hydrogenation bottle with 25 ml. of methanol. 2 g. of potassium hydroxide dissolved in 75 ml. of methanol and 10 g. of methyl 3-keto-bisnor-4-cholenate, prepared as in A, in 25 ml. of benzene and 50 ml. of methanol were added. This mixture was reduced with hydrogen. After 70 minutes, substantially 1 mol equivalent of hydrogen had been absorbed and the reaction was stopped.

The mixture wass filtered to remove catalyst and the filtrate was evaporated under vacuum to a slurry. The residue was diluted with water and extracted with ether. The ethereal solution was washed with successive portions of water, 5% aqueous potassium hydroxide and water. The washed solution was dried over sodium sulfate and evaporated to dryness. The residue was recrystallized from ether-petroleum ether. 7.35 g. of shiny white plates, m.p. 161° to 166° C., were obtained. This material showed no absorption in the ultraviolet.

After one recrystallization from ether-petroleum ether, the product, methyl 3-keto-bisnorcholanate, melted at 169° to 170° C.

Analysis: Calculated from $C_{23}H_{36}O_3$: C, 76.62; H, 10.05. Found: C, 76.62; H, 10.18; $(\alpha)_D^{25}$ (CHCl$_3$) = 16.4°.

EXAMPLE VI

Preparation of Etiochola-3,17-Dione-17-Ethylene Ketal

A) Preparation of the Ethylene Ketal of Dehydroandrosterone:

A mixture of 5 grams of dehydroandrosterone, m.p. 146° to 148° C., 0.3 grams of p-tosyl acid monohydrate, 100 cc. of dry benzene and 4.5 cc. of ethylene glycol was heated under reflux for 4 hours, excluding moisture from the system. The reaction mass was cooled, extracted with ether and the ether-benzene extract, after being washed with water, was dried over anhydrous sodium sulfate. The mass was evaporated to a syrup and crystallized by the addition of methanol. On standing about 16 hours in a cold place, the mass was filtered. 4.91 grams of crude ketal, m.p. 153° to 160° C., were obtained. Recrystallization from ether-methanol and from acetone increased the melting point to 166° to 167° C.

Analysis: For $C_{21}H_{32}O_3$. Calculated: C = 75.86%; H = 9.70%. Found: C = 75.60%; H = 9.63%.

B) Preparation of 4-Androstene-3,17-dione-17-Ethylene Ketal:

A mixture of 3.0 grams of the ketal prepared above in 120 cc. of toluene and 25 cc. of cyclohexanone was dried by distilling about 20 cc. of the mixture. To the remaining refluxing mass, 1.25 grams of aluminum isopropylate in 12 cc. of dried toluene were added dropwise in 10 minutes. After 30 minutes, 4 cc. of glacial acetic acid in toluene were added and the resultant mixture was distilled with steam for 1 hour.

The distilland was extracted with ether and the ether extracts were washed with dilute aqueous sodium hydroxide and with water until neutral. The extract, after being dried over anhydrous sodium sulfate, was evaporated to dryness. The oily residue was dissolved in a minimum quantity of a mixture of dry ether and petroleum ether. The solution was crystallized by seeding. 1.5 g. of first crop material, m.p. 114° to 146° C., were obtained. U.V. absorption spectra of this material showed a peak at 241 mμ, Emax = 16,400, indicating a 3-keto-Δ^4-system.

C) Reduction of 4-androstene-2,17-dione-17-ethylene ketal:

3 grams of the androstenedion-17-ethylene ketal dissolved in 30 cc. of benzene were reduced with a palladized charcoal mixture prepared from 9.6 cc. of 1% palladium chloride and activated charcoal, as described in Example I—A above, and in the presence of 0.6 grams of potassium hydroxide dissolved in 30 cc. of methanol. The reaction mixture was worked up in the usual manner and gave 2.54 grams of crude material. This, when recrystallized from ether-petroleum ether, melted at 112° to 114° C.

Analysis: For $C_{21}H_{32}O_3$. Calculated: C = 75.85%; H = 9.70%. Found: C = 75.98%; H = 9.63%.

The product comprising etiochola-3,17-dione-17-ethylene ketal of this example, upon reduction of the 3-keto group to 3α-hydroxy and hydrolysis of the ketal group with methanol and aqueous sulfuric acid, gives etiocholan-3α-ol-17-one melting at 144° to 145°

C.; $(\alpha)_D = +109$, compare J. Biol. Chem., *172*, 268 (1948).

EXAMPLE VII

Preparation of 5-Isostigmast-22-ene-3-one

A) Preparation of Stigmastadienone:

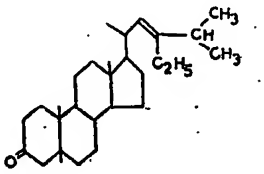
A mixture of 50 grams of stigmasterol, m.p. 167° to 168° C., 2000 cc. of toluene and 425 cc. of cyclohexanone was dried by distilling a portion of the solvent therefrom. To the boiling residue a solution of 21 grams of aluminum isopropylate in 200 cc. of toluene was added dropwise in 15 minutes. After ½ hour of refluxing, 5 cc. of glacial acetic acid in 20 cc. of toluene were carefully added and the resultant mixture was distilled with steam for about 1½ hours. The distilland was cooled and extracted with ether. The ether extract was washed with successive portions of 5% aqueous caustic soda, dilute acid and water. After being dried over anhydrous sodium sulfate, the ether solution is concentrated to a low volume. Upon addition of petroleum ether and chilling, the mass crystallized. In this manner, 40.9 g. of product, melting at 122° to 125° C., were obtained.

B) Reduction of stigmastadienone:

A solution of 10 grams of stigmastadienone in 100 cc. of benzene was mixed with 2 grams of 10% Pd-charcoal catalyst and 2 grams of potassium hydroxide in 100 cc. of methanol. The mixture was reduced with hydrogen under 30 psi. Within 7 minutes, and after the pressure had dropped by 2 psi, substantially 1 mol equivalent, the uptake of hydrogen ceased abruptly. The mass was diluted with 700 cc. of water after the catalyst had been filtered from the mixture, and the product was extracted with ether. The extracts were washed, dried and concentrated to a low volume. By the addition of methanol, the mass was caused to crystallize. 9.3 grams of material melting between 140° and 145° C. were obtained.

Analysis: For $C_{29}H_{48}O$. Calculated: C = 84.40%; H = 11.72%. Found: C = 84.48%; H = 11.93%.

The product of this example comprised 5-isostigmast-22-ene-3-one and upon reduction of the product with lithium aluminum hydride as described in copending application 32089/52, gave 5-isostigmasten-3α-ol, m.p. 150° to 153° C., 3α-acetate, 143° to 145° C. Upon ozonization of the 5-isostigmasten-3α-ol-acetate, 3α-acetoxy*bisnor*-lithocholic acid, m.p. 217° to 219° C., was obtained, compare Sawlwiez and Reichstein, Helv. *20*, 949 (1937). The structure of 5-isostigmast-22-ene-3-one is



It can be readily seen from the foregoing that a clean-cut stereospecific procedure for the preparation of 3-keto-A/B-cis steroids is provided, and that this novel process is of value in converting derivatives of vegetal sterols such as stigmasterol and diosgenin to compounds having the spatial configuration at the junction of rings A and B of many of the steroids derived from animal sources. Further, as disclosed in copending application 32089/52 (Serial No. 736,817) the 3-keto group of these compounds can be reduced with lithium aluminum hydride to a 3α-hydroxyl substituent, thereby extending the stereochemical conversion of more abundant and/or readily obtainable 3β-A/B-trans steroids characteristic of derivatives from vegetal steroids to the 3α-A/B-cis configurafion characteristic of many derivatives of animal steroids whose availability is relatively limited, e.g., desoxycholic acid.

The process has been illustrated by examples in which the reduction has been carried out in the presence of caustic alkalis. While this type of alkaline reagent is preferred, other inorganic bases can be used, for example, alkali metal carbonates such as sodium carbonate, alkali metal phosphates such as sodium tetraphosphate, and potassium pyrophosphate. Preferably, a concentration of the inorganic base of about 20% by weight of the 3-keto-Δ^4-steroid is used.

We have found that this reduction occurs readily at low pressures, i.e., below 5 psi, and for convenience we prefer to operate at atmospheric or slightly above, but higher pressures can be used. Further, in view of the sensitivity of many steroid derivatives to alkali, we prefer, particularly when using a caustic alkali, to conduct the hydrogenation at below 50° C. and especially at from about 20° C. to about 30° C.

It is not necessary to employ methyl esters only, as other esters than methyl, such as the ethyl or butyl ester, and esters containing the benzoyl, hemisuccinoyl or naphthoyl group may be employed. Also other cyclic ketals than the ethylene ketal may be employed. Preferably, however, the ketals are those which possess 3 or 4 carbon atoms in the cyclic ketal ring, i.e., those prepared from hydroxy compounds in which the OH groups are 1,2 or 1,3 to each other.

What we claim is:—

1. A process of reducing 3-keto-Δ^4-steroids which comprises treating a 3-keto-Δ^4-steroid (excluding steroids containing an 11-keto group) with hydrogen in the presence of palladium catalyst and in the presence of an inorganic base and in an anhydrous medium to reduce the 4-5 double bond to form 3-keto-A/B-cis-steroids substantially free of the allo isomers.

2. A process according to claim 1, which comprises treating a 3-keto-10,13-dimethyl-Δ^4-steroid.

3. A process according to claim 1 or 2, in which the reaction is carried out at low pressures i.e. below 5 lbs. per sq. in.

4. A process according to any one of the preceding claims, in which the reaction is carried out at a temperature below 50° C.

5. A process according to claim 1 or 2, in which the reaction is carried out at atmospheric pressure and at a temperature of from about 20°C. to about 30°C.

6. A process according to any one of claims 1—5, in which the starting steroid is a pregnene.

7. A process according to any one of claims 1—5, in which the starting material also contains a double bond in the 7-8 position.

8. A process according to any one of claims 1—5, in which the starting material is a stenone.

9. A process according to any one of claims 1—5, in which the starting material is a steroid of the C_{19} series.

10. A process according to any one of claims 1—5, in which the starting material is a steroid of the C_{22} series.

11. A process according to any one of the preceding claims, in which the inorganic base is a caustic alkaline medium.

12. A process according to any one of claims 1—10, in which the inorganic base is sodium carbonate.

13. A process according to claim 1, in which the 3-keto group is the sole keto group attached to the polyhydrocyclopentanophenanthrene nucleus of the steroid.

14. A process of preparing a 3-keto-A/B-cis steroid which comprises the step of hydrogenating an ester of 3-keto-bisnor-4,7-choladienic acid or 3-keto-bisnor-4-cholenic acid in the presence of a palladium catalyst and in the presence of an inorganic base and in an anhydrous medium to yield the esters of 3-keto bisnor-7-cholenic acid or 3-keto-bisnor-cholanic acid respectively.

15. A process of preparing Δ^7-A/B-cis pregnene compounds which comprises the step of hydrogenating $\Delta^{1,7}$-pregnadiene-dione-3,20 and the 20-cyclic ketal derivatives thereof derived from alkylene glycols in the presence of a palladium catalyst, and in the presence of a basic material and in an anhydrous medium to yield 3-keto-Δ^7-pregnendione-3,20 and the 20 cyclic ketals.

16. Δ^7-pregnene-3,20-dione.

17. 3-keto-bisnor-Δ^7-cholenic acid and esters thereof.

18. The process of reducing 3-keto-Δ^4-steroids to reduce the 4,5 double bond substantially as herein described with reference to the Examples.

STEVENS, LANGNER, PARRY & ROLLINSON,
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Agents for the Applicants.

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